

[00062] Blended or non-blended polyurethanes are particularly preferred membrane materials. Tecophilic®, a high water uptake, medical grade, aliphatic, polyether polyurethane, manufactured by Thermedics Inc., Woburn MA, is a particularly preferred membrane material.

[00063] Preferred membrane functionality according to this embodiment such as water uptake and water permeability can be obtained by either blending low and high water uptake materials or by direct synthesis of materials of varying water uptake. For example, Tecophilic consists of aliphatic “hard segments” and different proportions of polyethylene glycol (PEG) and polytetramethylene glycol (PTMG) “soft segments”, which proportions of PEG and PTMG can be varied during polymer synthesis to provide the desired water uptake and water permeation. Generally, higher water uptake and higher permeability materials comprise a higher proportion of PEG. Various materials for the fabrication of the other components of the fluid-imbibing device of Fig. 4 are known in the art or are disclosed in the aforementioned patents previously incorporated by reference.

[00064] Preferred annealing temperatures according to this embodiment are about 50°C - 100°C, preferably about 50°C - 80°C, and most preferably about 55°C - 75°C. The annealing time is about 1-250 hours, preferably about 4 - 72 hours, and most preferably about 12 - 48 hours. Prior to annealing, the membranes are stored at room temperature for relaxation, preferably for at least 12 hours - 7 days, and more preferably for at least about 2 - 3 days after processing. The combination of allowing time for membrane relaxation followed by annealing result in the membrane achieving steady-state functionality at a much quicker rate. Membrane annealing according to this embodiment also enhances the mechanical strength of the membrane.

[00065] It is believed that this invention has utility in connection with the delivery of a wide variety of drugs. It is to be understood that more than one drug may be delivered by the devices of this invention. For example, suitable

drugs for administration by the devices of this invention are disclosed in the aforementioned patents and patent applications previously incorporated by reference. In general, practice of this invention includes devices to be used to deliver therapeutic drugs in all of the major areas, including, but not limited to, ACE inhibitors, adenohipophyseal hormones, adrenergic neuron blocking drugs, adrenocortical steroids, inhibitors of the biosynthesis of adrenocortical steroids, alpha-adrenergic agonists, alpha-adrenergic antagonists, selective alpha-two-adrenergic agonists, analgesics, antipyretics and anti-inflammatory drugs, androgens, local and general anesthetics, antiaddictive drugs, antiandrogens, antiarrhythmic drugs, antiasthmatic drugs, anticholinergic drugs, anticholinesterase drugs, anticoagulants, antidiabetic drugs, antidiarrheal drugs, antidiuretic, antiemetic and prokinetic drugs, antiepileptic drugs, antiestrogens, antifungal drugs, antihypertensive drugs, antimicrobial drugs, antimigraine drugs, antimuscarinic drugs, antineoplastic drugs, antiparasitic drugs, antiparkinson's drugs, antiplatelet drugs, antiprogestins, antithyroid drugs, antitussives, antiviral drugs, atypical antidepressants, azaspirodecanediones, barbituates, benzodiazepines, benzothiadiazides, beta-adrenergic agonists, beta-adrenergic antagonists, selective beta-one-adrenergic antagonists, selective beta-two-adrenergic agonists, bile salts, drugs affecting volume and composition of body fluids, butyrophenones, drugs affecting calcification, calcium channel blockers, cardiovascular drugs, catecholamines and sympathomimetic drugs, cholinergic agonists, cholinesterase reactivators, dermatological drugs, diphenylbutylpiperidines, diuretics, ergot alkaloids, estrogens, ganglionic blocking drugs, ganglionic stimulating drugs, hydantoins, drugs for control of gastric acidity and treatment of peptic ulcers, hematopoietic drugs, histamines, histamine antagonists, 5-hydroxytryptamine antagonists, drugs for the treatment of hyperlipoproteinemia, hypnotics and sedatives, immunosuppressive drugs, laxatives, methylxanthines, monoamine oxidase inhibitors, neuromuscular blocking drugs, organic nitrates, opioid analgesics and antagonists,

pancreatic enzymes, phenothiazines, LHRH and its analogues such as leuprolide, progestins, prostaglandins, drugs for the treatment of psychiatric disorders, retinoids, sodium channel blockers, drugs for spasticity and acute muscle spasms, succinimides, thioxanthines, thrombolytic drugs, thyroid drugs, tricyclic antidepressants, inhibitors of tubular transport of organic compounds, drugs affecting uterine motility, vasodilators, vitamins and the like.

[00066] The following examples are offered to illustrate the practice of the present invention and are not intended to limit the invention in any manner.

EXAMPLE 1

[00067] Transdermal therapeutic systems comprising an aqueous ethanolic gel were prepared according to the following procedure. Fentanyl base was added to a mixture of 95% ethanol and purified water. 2% of hydroxyethyl cellulose gelling agent was added slowly to the solution with stirring and mixed until a smooth gel was obtained (approximately 1 hour). A 0.05 mm thick contact adhesive layer was formed on a release liner for the system by solution casting an amine resistant silicone medical adhesive (XCF 2992, Dow Corning, Midland MI) onto the polyester film from a solution in heptane.

[00068] An annealed or non-annealed rate controlling membrane comprised of EVA (9% VA) was pressure laminated to the exposed adhesive as set forth in the system configuration shown in Table 1 below. The rate controlling membranes subjected to an annealing process according to this invention (systems 2 and 4) were maintained at about 60° C for a period of time of about 24 hours and subsequently allowed to cool to ambient conditions for 2 days before being pressure laminated to the adhesive.